GEIS Respiratory Disease Surveillance Newsletter
DoD Center for Deployment Health Research
Naval Health Research Center, San Diego

Issue 3 February 2001

Background – Sponsored by the DoD Global Emerging Infections System (GEIS), the Naval Health Research Center (NHRC) is collaborating with numerous federal and non-federal institutions conducting surveillance for several respiratory pathogens (adenovirus, influenza, respiratory syncytial virus (RSV), parainfluenza, *Streptococcus pyogenes*, and invasive *Streptococcus pneumoniae)*. We are also developing some new studies, which are detailed in the "What's New" section below. Additional information may also be found at www.nhrc.navy.mil/geis

What's New?

Upcoming Conferences

- **Recruit Healthcare Symposium 2001** April 17-20, San Antonio, TX
- **Navy Occupational & Preventive Medicine Workshop**, May 11-18, San Diego, CA
- **4th Annual Conference on Vaccine Research,** April 23-25, Arlington, VA
- **Women in Military Service: research for health for today & tomorrow**, September 20-21, Washington, DC

New Publications

- Adult adenovirus infections: Loss of orphaned vaccines precipitates military respiratory disease epidemics, Gray GC, et al. *Clin Infec Dis*, **in press**
- Adenovirus vaccine cost effectiveness, Hyer R, Ryan M, Gaydos J. ***Am J Trop Med Hyg*, in press**
- A modified rapid method of nucleic acid isolation from suspension of matured virus: Applied in restriction analysis of DNA from an adenovirus prototype & patient isolate, Le CT, Gray GC, Poddar SK. ***J. Med Microbiology*, in press**

New NHRC-GEIS Proposals

- **Are Adenovirus Infections Among Military Personnel Associated with the Development of Obesity?** Proposed case control study to determine if an association exists between weight control problems (obesity) and adenovirus-36 exposure in a population of active duty Navy personnel in the San Diego area.

NHRC Job Openings

- Molecular Lab Technician, Molecular Consultant
- Director, Respiratory Disease Laboratory
- Director, Epidemiologist
- Director, Statistician
- Research Assistant, Fort Jackson and MCRD Parris Island

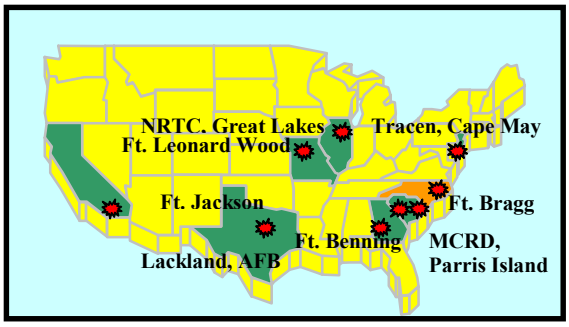
Study Updates:

Flu Diagnostic. The evaluation of two rapid influenza tests has resumed at 3 Army training centers (Ft. Benning, Ft. Jackson, & Ft. Leonard Wood). Influenza B was cultured in several recent specimens, which will allow more precise measurement of the test's sensitivities. Testing is scheduled to continue through March 2001.

Pneumococcal Study In collaboration with Wyeth-Lederle vaccines, NHRC and 4 recruit training sites will conduct a double blind, placebo-controlled trial of a 23-valent pneumococcal vaccine. The study is currently underway at Fort Leonard Wood, and NRTC, Great Lakes. Fort Jackson began specimen collection at the end of January, and MCRD Parris Island will begin specimen collection soon thereafter. The study will enroll 191,000 trainees and follow them over a period of 24 months for respiratory disease. To date, study site personnel have enrolled more than 8500 recruits with a better than 69% enrollment rate.

ZymeTx Rapid Flu Diagnostic. A two-year clinical trial comparing the sensitivity/specificity of two rapid influenza diagnostic tests (ZymeTx, ZstatFlu ® and Quidel, QuickVue®) to viral culture will begin in January at the Ambulatory Care Center, Point Loma, CA. Military medical beneficiaries who are over the age of 18 years old and who meet the case definition for FRI will be eligible to participate. Data collection is scheduled to begin in February 2000.

Febrile Respiratory Illness Surveillance Sites



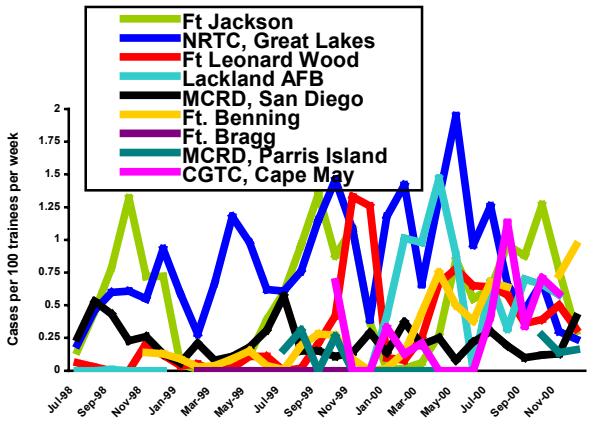
Adenovirus

Current Progress - Adenovirus remains the leading cause of febrile respiratory illness (FRI) among trainees. More than 60% of the 6454 throat cultures collected between June 1998 and December 2000 were positive for adenovirus. Unvaccinated trainees (n=5698) were more likely to be adenovirus positive (OR=2.17, 95% CI 1.65-2.85) than vaccinated trainees who received only type 7 vaccine (n =234). More than 97% of the adenovirus positive specimens (n =3599) came from unvaccinated personnel. More than 94% of the recent adenovirus isolates have been type 4.

Geographic Trends - In 1999 and 2000, six of the eight surveillance sites reported "historic" epidemic threshold (1.50 cases per 100 trainees per week) FRI rates (Figure 1). Please note that due to low yield, specimen collection was terminated at the Fort Bragg site in March 2000. The amount of FRI morbidity caused by adenovirus varied by location ranging from 4.8% at Fort Bragg, to 76.4% at MCRD, San Diego (Figure 2). See below for rates.

Temporal Trends - Epidemic threshold FRI rates were observed at the sites during each season in the year 2000, peaking in the spring and fall months. This is in contrast to historically described seasonal trends, which were primarily winter months. Epidemic threshold FRI rates were also observed during each month of the year 2000 (Figure 1).

Adenovirus Infection Rates at Basic Training Sites



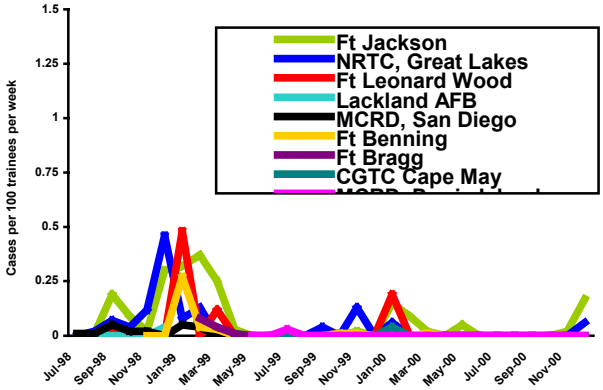
Influenza

Current Progress - As of December 30, 2000, 341 (5.3%) of the 6454 FRI specimens tested were positive for influenza (4.2% type A and 1.1% type B). Please see next column for monthly rates. Trainees who were not vaccinated against influenza, were more than 3 1/2 times more likely to be influenza-positive (OR= 3.61, 95% CI, 2.83-4.61). During the period of November 2000 to January 2001, 325 FRI specimens were tested. Of the 325 tested specimens, 4.6% were identified with influenza as the responsible pathogen. Surveillance data collected thus far indicate that influenza types A/New Caldonia/20199-like and B/Yamanashi/166-like were most prevalent during this flu season (2000 -2001). However, adenovirus remained the most prevalent FRI etiology (proportional distribution shown in Figure 3).

Geographic Trends – The morbidity caused by infection with influenza A or B varied by location. During the 1999-2000 flu season (months of December thru March), influenza isolation ranged from 0% at Lackland AFB, to 30.0% at Fort Bragg. During the 2000-2001 flu season, 11.4% of the 88 specimens tested from Ft. Jackson were positive for either influenza A or B.

Temporal Trends – During the period of 1/99 to 6/99, there were more than twice as many cases of influenza identified (n=196) as compared with 1/00 to 6/00 (n=66, Figure 4). The percentage of unvaccinated trainees was 38% during 1999 and 19% in 2000. Data from multiple surveillance institutions indicate that influenza (within the United States) was most prevalent during the winter and spring months.

Influenza Infection Rates at Basic Training Sites



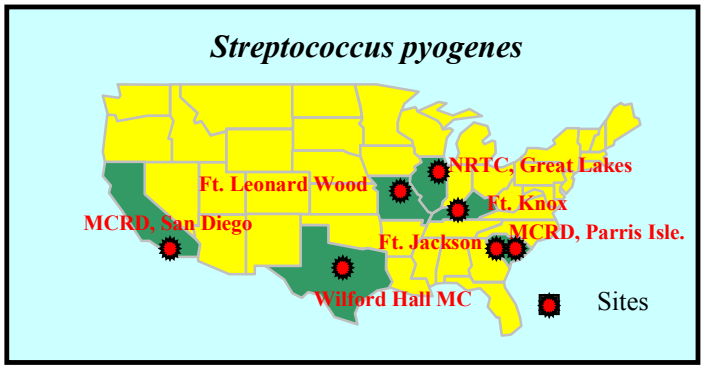
Other Pathogens – Of the 6,454 throat cultures tested, 21 (0.3%) were positive for RSV and 73 (1.4%) grew parainfluenza 1, 2, or 3.

FRI specimens tested per site 6/98 to 12/00

SITE	SPECIMENS TESTED
Fort Benning	918
Fort Bragg	63
Fort Jackson	2191
Fort Leonard Wood	993
NRTC, Great Lakes	904
MCRD, San Diego	528
MCRD, Parris Island	213
CGTC Cape May	286
Lackland AFB	358

Rapid Influenza Diagnostic Testing (Quidel/BioStar)

Current Progress - We are evaluating 2 rapid diagnostic influenza tests in comparison with standard viral culture testing, BioStar FluOIA® and Quidel QuickVue®. Both tests are immunoassays that detect nucleoprotein antigens found in influenza A and B. These point-of-care tests provide results within 30 min, allowing for antiviral treatment of influenza-positive patients and reducing the inappropriate use of antibiotics. Between February and May 2000, 228 trainees with FRI symptoms were enrolled at 3 recruit training centers. Preliminary results show that the FluOIA and QuickVue specificity's were 54% and 86%, respectively. Sensitivity could not be measured because only 1 culture-positive specimen was found. The study resumed in November 2000, and we have begun to see more culture-positive influenza recently.



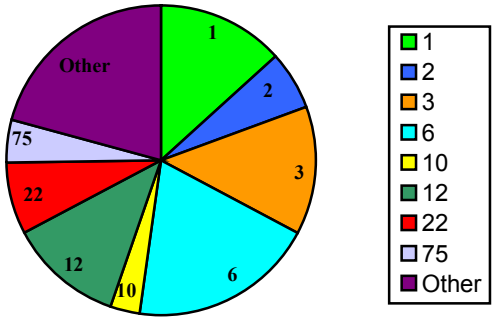
Streptococcus pyogenes

Current Progress – *Streptococcus pyogenes* (Group A streptococcus) continues to be a threat to the health of military trainees. Between 2/98 and 02/01, 363 clinical isolates were collected from trainees at 8 military sites.

Antibiotic Resistance – *S. pyogenes* maintains 100% susceptibility to three antibiotics (penicillin, levofloxacin, and vancomycin). Fifty-three (14.6%) of the 363 isolates collected had full or partial resistance to erythromycin, 34 (9.4%) to tetracycline, and 11 (3.0%) to clindamycin (Figure 5). Nine (2.5%) of the isolates were resistant to both erythromycin and tetracyline. Isolates from female (n=55) trainees exhibited a greater proportion of erythromycin resistance as compared to male trainees (18.2% and 14.2%, respectively).

Emm-gene Types – The most common emm-gene types (n=67) for *S. pyogenes* among military trainees were 6 (20.9%), 1 (13.4%), 3 (13.4%), 12 (11.9%), 22 (7.5%), 2 (7%), and 75 (4.5%). These seven emm-gene types made up more than 78% of all the typed isolates.

Emm-Gene Type Distribution of Streptococcus pyogenes Isolates Among U.S. Military Trainees

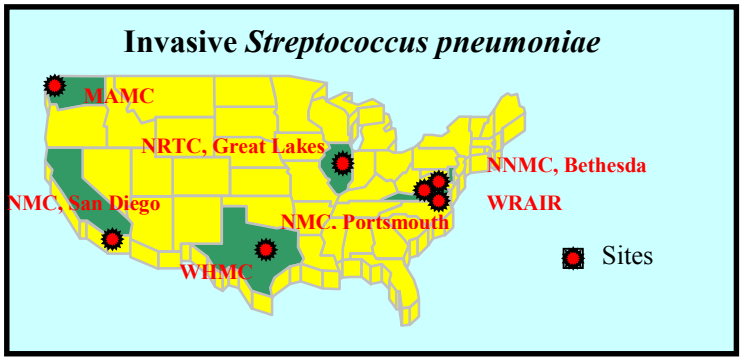


Resistance by Emm-gene type – Erythromycin resistance varied by emm-gene type. Type 22 (80%) demonstrated the most erythromycin resistance of all emm-gene typed isolates (Figure 6).

Geographic Trends – *S. pyogenes* isolates from military trainees currently maintain high susceptibility to many commonly prescribed antibiotics. However, we continue to observe an unequal geographic distribution of erythromycin resistance at the sites. Resistance to erythromycin ranged from 0% at Fort Jackson to 32.4% at Lackland AFB. Additionally, 30 of the 102 (29.4%) isolates submitted by Lackland AFB were fully resistant to erythromycin.

***S. pyogenes* isolates received per site 2/98 to 02/01**

SITE	ISOLATES RECEIVED
NRTC, Great Lakes	89
MCRD, Parris Island	87
Fort Jackson	4
Fort Knox	23
Fort Leonard Wood	35
Fort Sill	19
Lackland, AFB	102



Streptococcus pneumoniae

Current Progress – Testing is complete for 271 invasive clinical isolates collected between 8/97 and 02/01 from military healthcare beneficiaries at 7 military medical centers.

Antibiotic Resistance – Eighty-nine (32.8%) of the 271 isolates collected had full or partial resistance to penicillin, and 61 isolates (22.5%) exhibited resistance to three or more antibiotics (Figure 7). Males (57.2%) and females (42.8%) exhibited similar resistance patterns. Similar patterns of penicillin-resistance were observed across all age groups. A majority of the penicillin resistant isolates came from those in the ≤=1 and ≥ 66 years age groups.

Invasive *S. pneumoniae* Penicillin Resistance by Age Group

Age	# Tested	Susceptible	Intermediate	Resistant
≤ 1	81	61%	27.20%	12.30%
2-65	112	73.2	17.0	9.8
≥ 66	27	63.0	7.4	29.6

Geographic Trends – We observed an unequal geographic distribution of penicillin resistance. Penicillin resistance ranged from 0% at NRTC, Great Lakes to 45.8% at Walter Reed Army Medical Center, although the number of isolates contributed by each site was not evenly distributed.

***S. pneumoniae* Serotypes** - Of the 124 typed isolates, the most common serotypes were 14 (23%), 6 (15%), 19 (15%), 9 (13), 4 (12%), 23 (9%), and 18 (4%) (Figure 8), all of which are included in the 23-valent pneumococcal vaccine. These seven serotypes made up more than 90% of the typed isolates at the sites. Four of the serotyped isolates came from vaccinated individuals.

Resistance by Serotype - Penicillin resistance differed by serotype with types 19 (69.2%), 9 (56.2%), and 6 (52.6%) having the most resistance. These three serotypes accounted for more than 74% of all penicillin resistance among the serotyped isolates, though they only accounted for 42% of the serotypes. Additionally, the distribution of *S. pneumoniae* serotypes differed by age group (Figure 9).

Temporal Trends - Overall, the number of invasive *S. pneumoniae* isolates at the medical centers increased moderately during the fall and winter and decreased during the spring and summer months.

***S. pneumoniae* isolates tested per site 8/97 to 01/01**

SITE	ISOLATES RECEIVED
NRTC Great Lakes	4
Naval Med. Ctr (NMC), San Diego	76
NMC, Portsmouth	2
National Naval Med. Ctr (NNMC), Bethesda	12
Walter Reed AIR	24
Wilford Hall MC	65
Madigan Army Med. Ctr. (AMC)	88

Bordetella pertussis

Current Progress - Surveillance of *Bordetella pertussis* is currently underway at 3 military recruit training sites, MCRD, San Diego, Ft. Benning, Ft. Leonard Wood). The NRTC, Great Lakes site will begin specimen collection in February 2001. To date, 80 specimens from recruits meeting the case definition (≥7 days of cough and symptoms consistent with respiratory infection) have been collected and tested using conventional culture method. Preliminary results indicate that at least one (1.3%) of the specimens tested positive for the pathogen. Additionally, 35 specimens have been tested by PCR, and of those tested, 4 (11.4%) were positive for *B. pertussis*. The serology component of this study is has not yet begun.

***B. pertussis* isolates tested per site**
6/00 to 1/01

SITE	ISOLATES RECEIVED
MCRD, San Diego	50
Ft Leonard Wood	30
Ft Benning	0
NRTC Great Lakes	Start 2/01

We welcome any comments or suggestions you may have regarding the information contained in this newsletter. For additional information, please contact the newsletter staff.

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***Final Note - As always, we'd like to thank the staff at the participating surveillance sites and collaborating institutions. This newsletter would not be possible without your hard work and dedication to excellence!**

Figure 1.

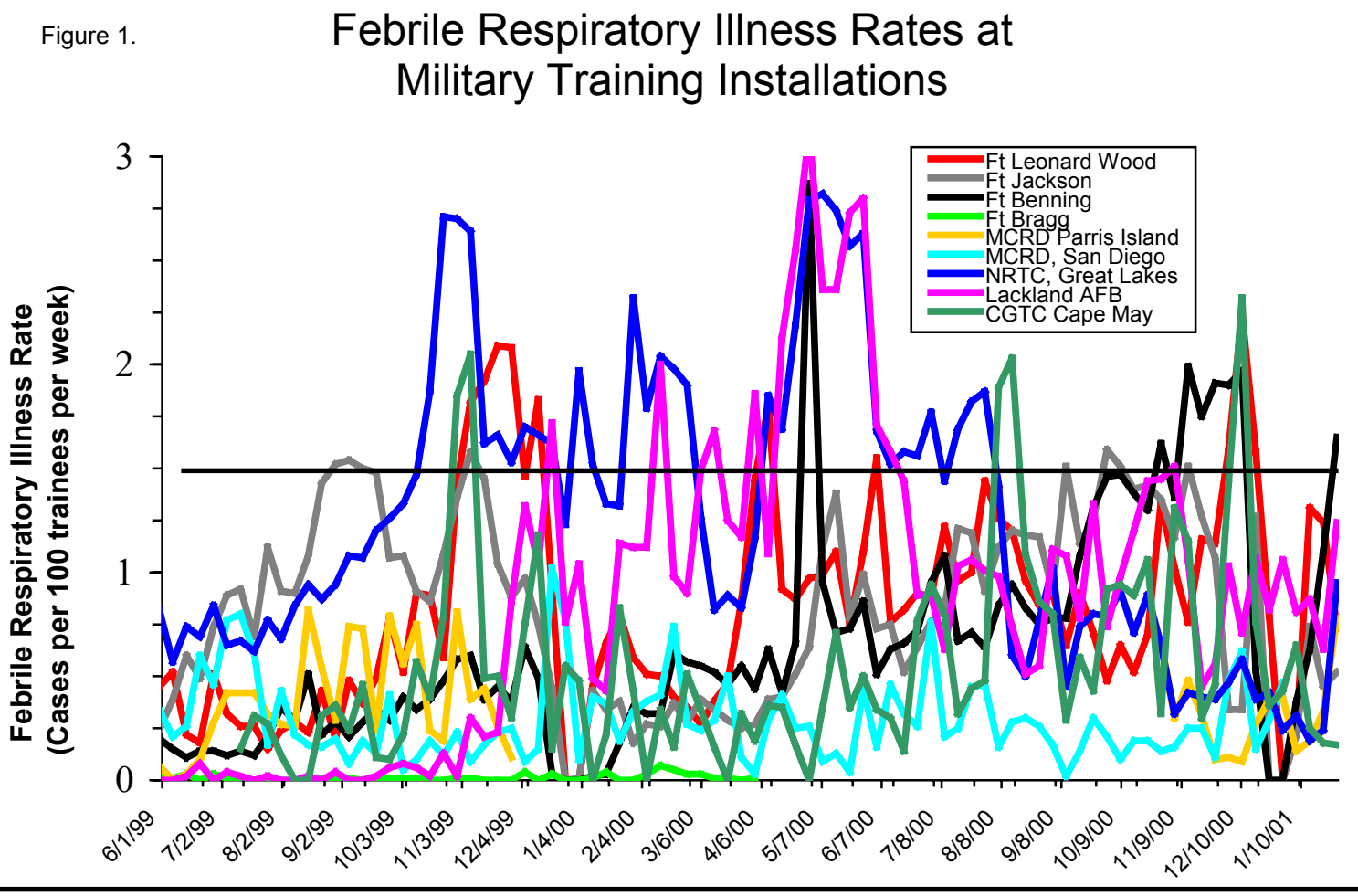


Figure 2.

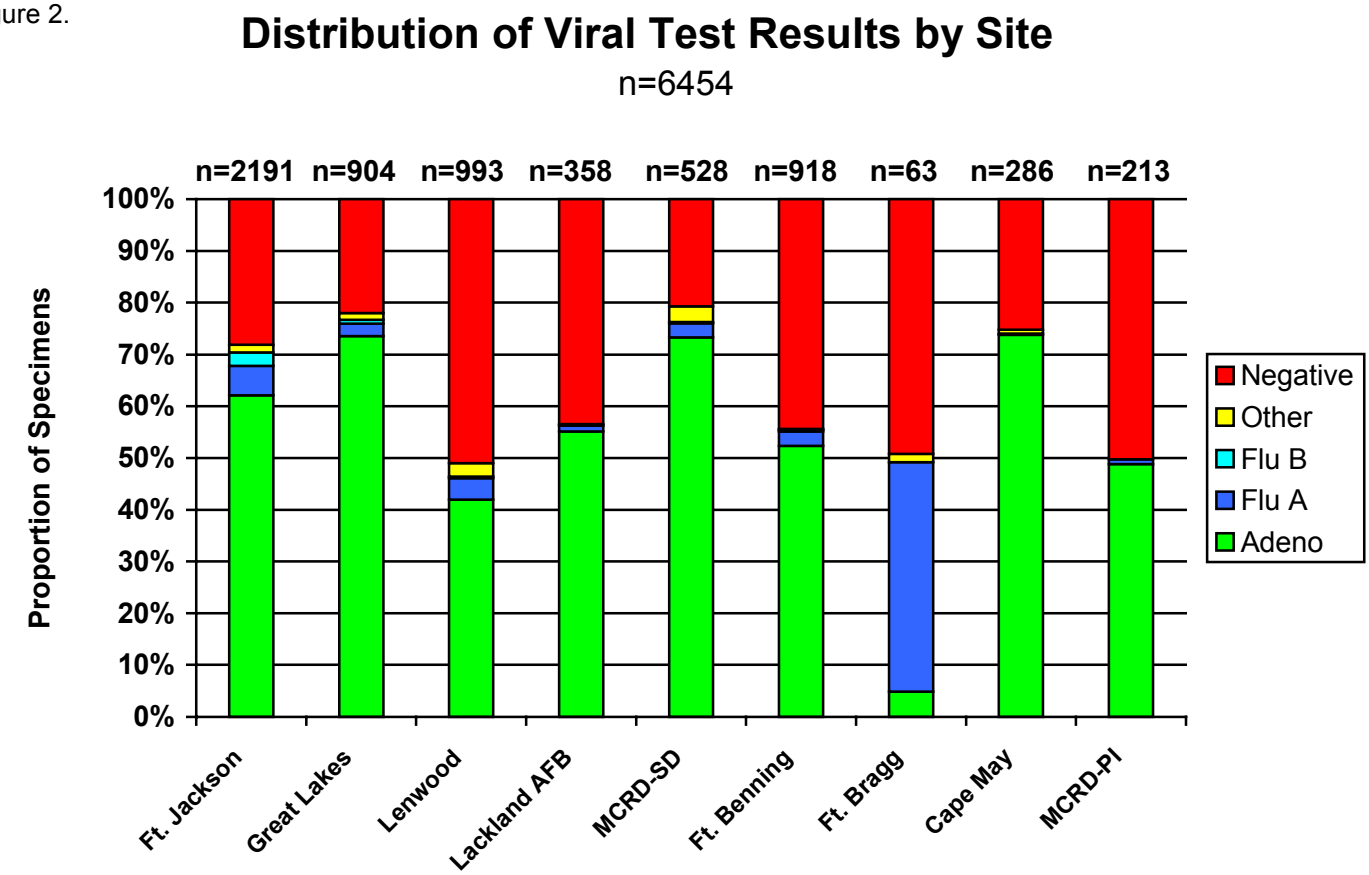
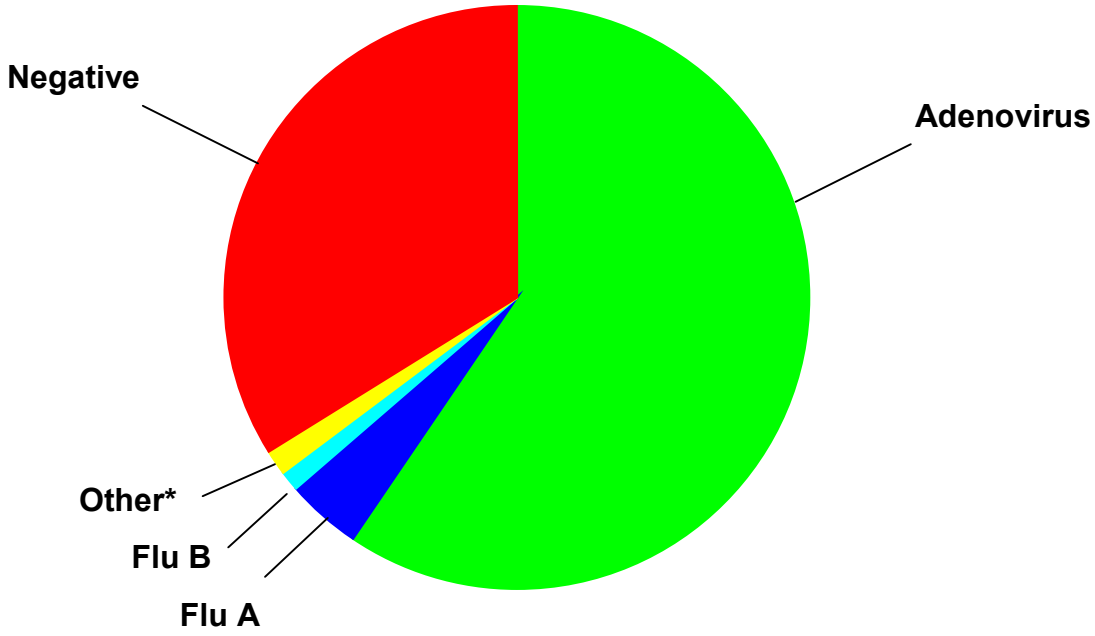


Figure 3.

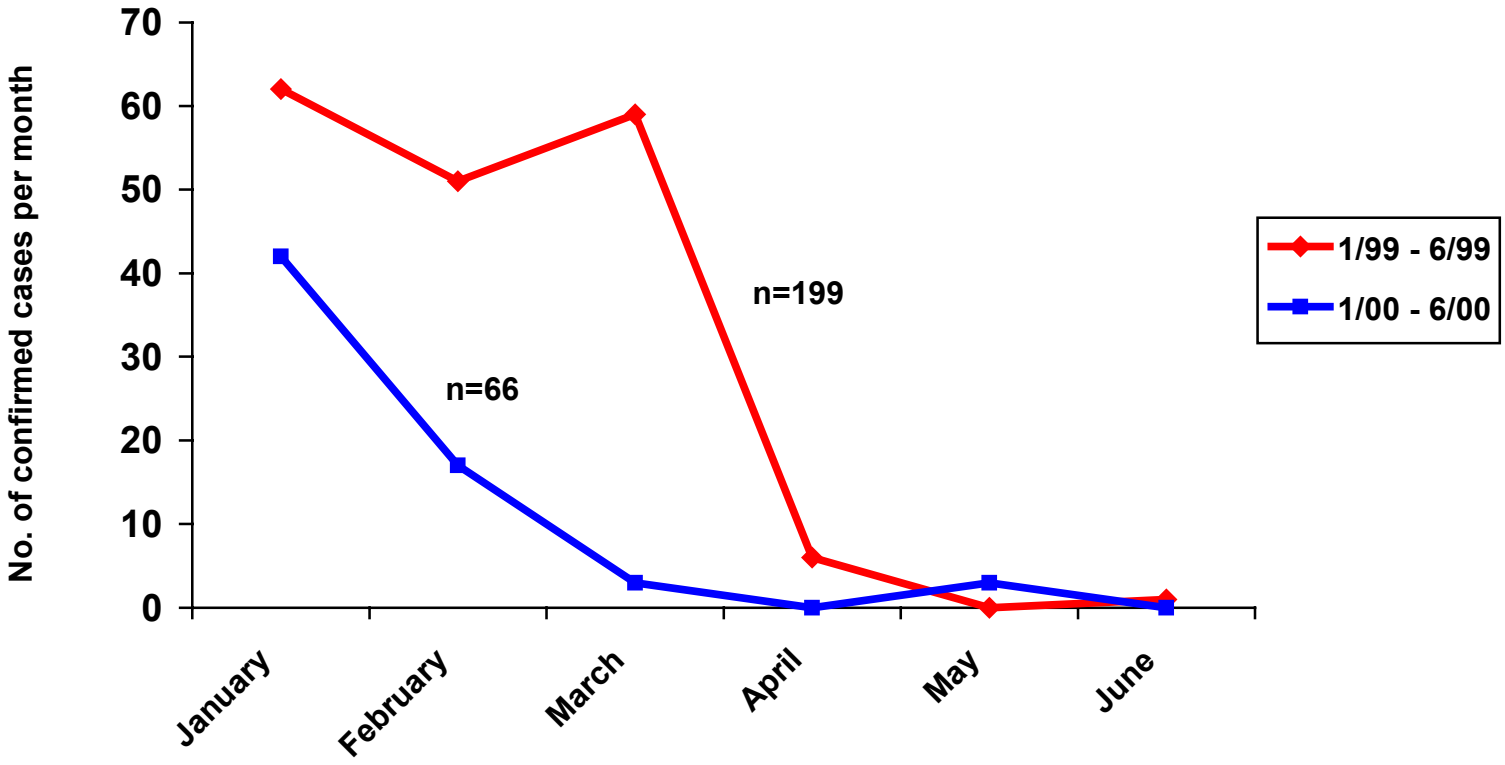
Proportional Distribution of Viral Test Results from June1998 to December 2000 (n=6454)



*RSV and parainfluenza 1, 2, and 3

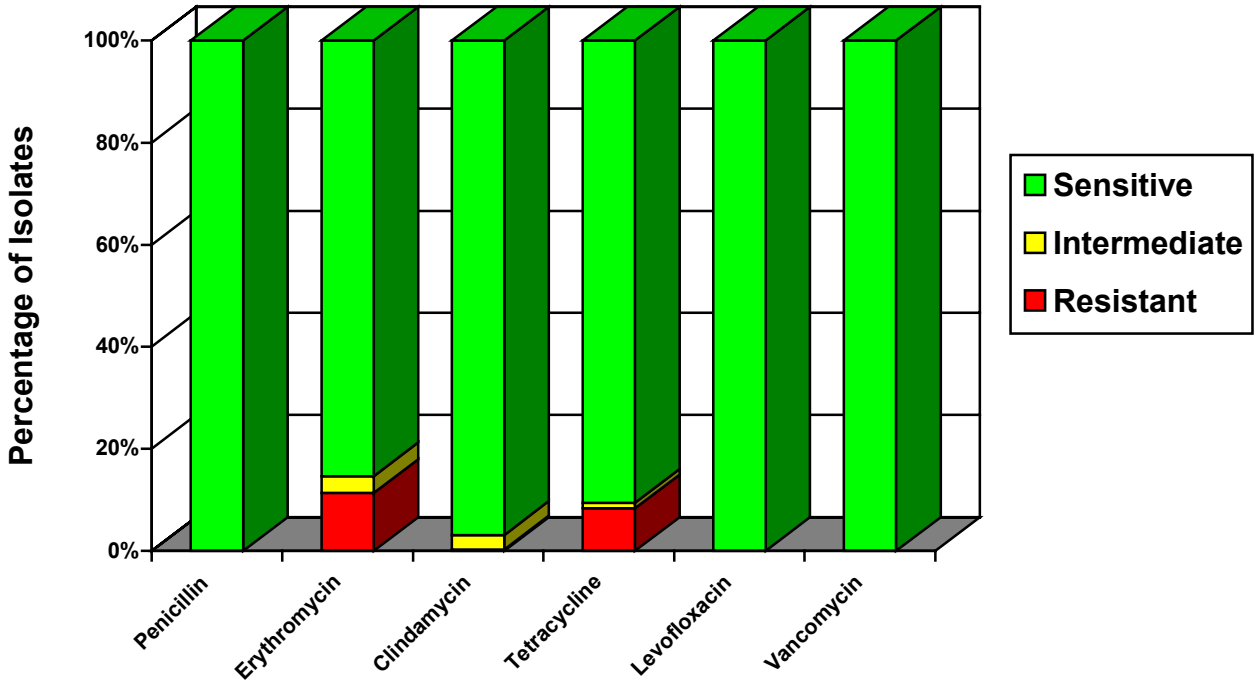
Figure 4.

1999/2000 Influenza-Positive Test Results Over Time



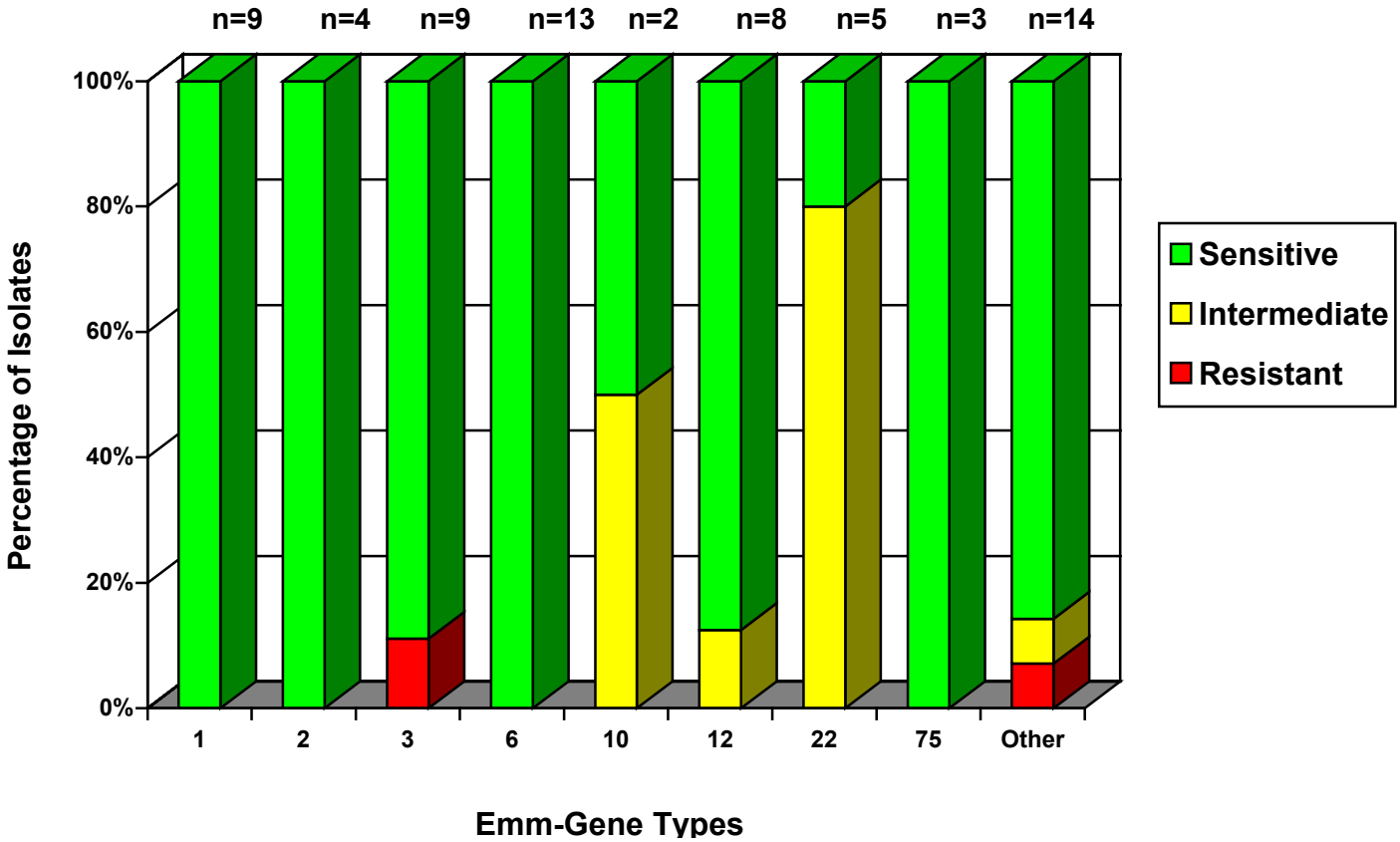
n=265 influenza-positive isolates from 1/99 to 6/99 and 1/00 to 6/00

Figure 5. Antibiotic Resistance Patterns of Clinical *S.pyogenes* Isolates from Military Trainees



n=363 isolates collected between 2/98 and 02/01

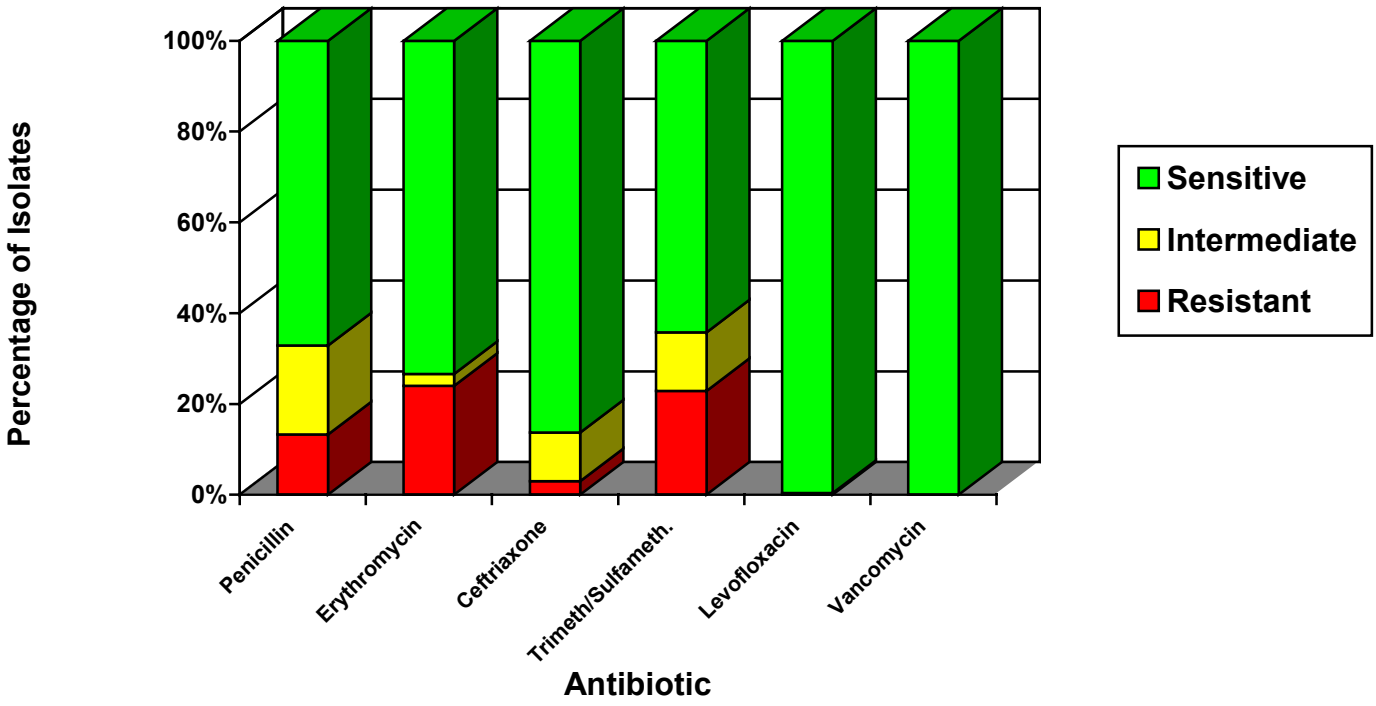
Figure 6. Erythromycin Resistance Patterns by Emm-gene Type Distribution of *S. pyogenes* Isolates



n=67 Emm-gene typed isolates collected between 2/98 and 6/00

Figure 7.

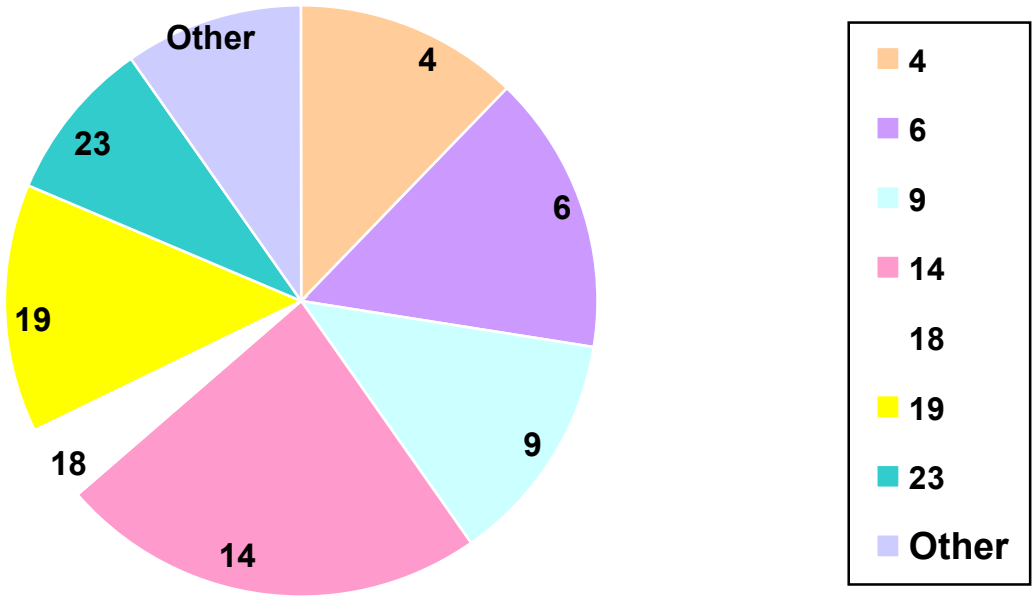
Antibiotic Resistance Patterns of Sterile Site *S. pneumoniae* Isolates From Military Medical Facilities



n=271 isolates collected between 8/97 and 02/01

Figure 8.

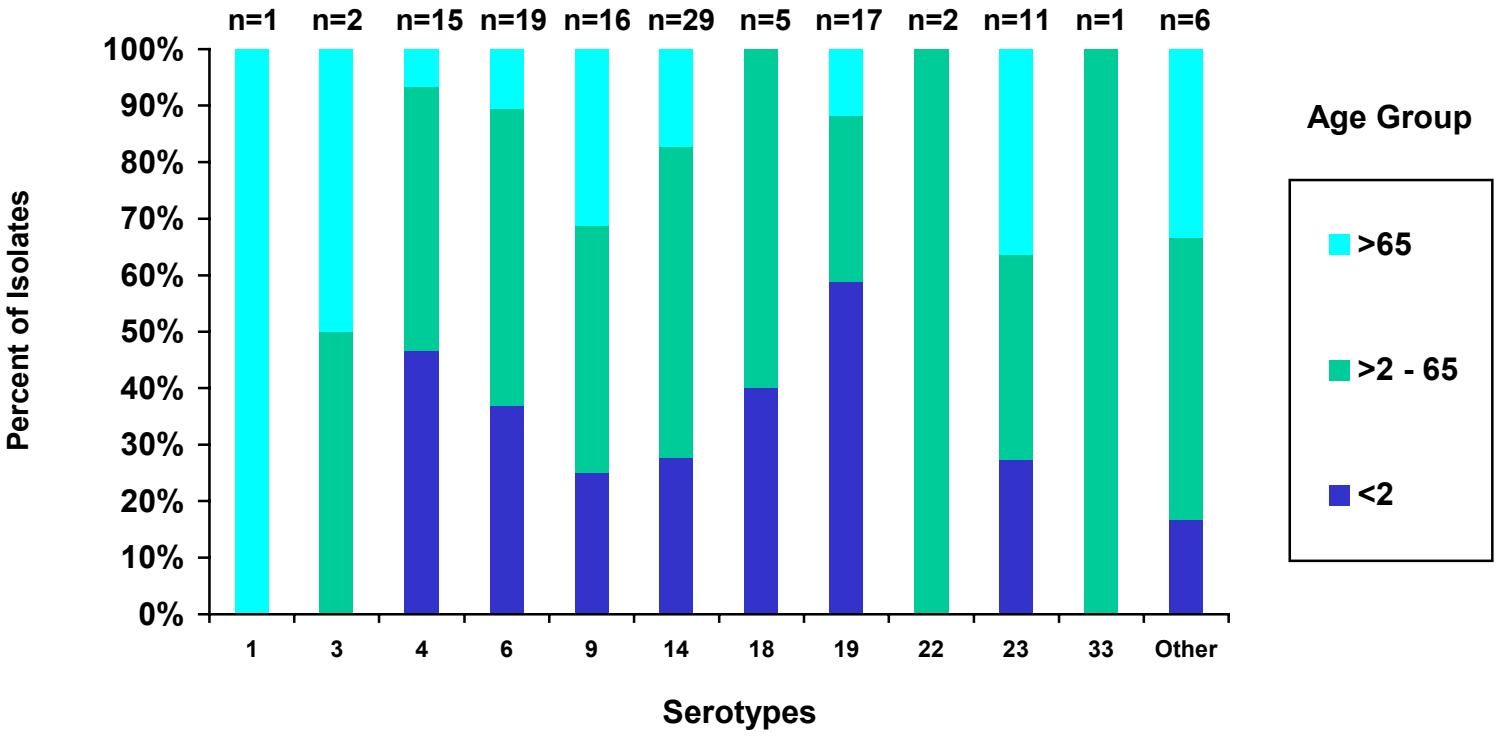
Serotype Distribution Patterns of Sterile Site *S. pneumoniae* Isolates



n=124 serotyped isolates collected between 8/97 and 6/00

Figure 9.

Distribution of Sterile Site *S. pneumoniae* Serotypes by Age Group



n=124 serotyped isolates collected between 8/97 and 6/00
*Please note - 1 serotyped isolate does not have age data